Effects of pirbuterol and sodium nitroprusside on pulmonary haemodynamics in hypoxic cor pulmonale

pioneers like Pearl Kendrick, Margaret Pittman, L B Holt, and members of the WHO group, and I gave relevant references. If Dr Preston objects, he should refute their work not mine. He might also take issue with Dr Griffith, who says (and I do not doubt it) that his company's vaccine contained all the main antigens from 1964 or earlier. Addition of antigen 3 to all British vaccines did not stop the major outbreaks of 1967-8, 1970-1, or 1974-5 during a period when vaccine acceptance was much higher than it is now; nor did it bring any change in the fact that 25-35% of proved cases, now as well as then, occur in fully vaccinated children not only in Britain but also in the United States,[1] Canada,[2] Australia,[3] Sweden,[4] and elsewhere. In parts of Scotland in 1977-9 the incidence of whooping cough in fully vaccinated children exceeded this range,[5 6] and it could be argued that the loss of immunity two to three years after vaccination is the main determinant of the otherwise unexplained 44 month periodicity of outbreaks of whooping cough in Britain (personal report to Department of Health and Social Security).

I imagine that most of your readers are bored, confused, or exasperated by the continuing controversy about this one, relatively unimportant infection and its relatively ineffective vaccine, which is disproportionately important because so many children receive it. Might I therefore state yet again the central plea in my own argument for the need to repair "the national deficit in epidemiological data and intelligence,"[5] because without some improvement, and not only about pertussis vaccine, we are abusing the trust of the public in medical judgment and in medicaments.

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[1] Pertussis surveillance, Georgia. *MMWR* 1977;**26**: 307-8.
[2] Mathias RG. Whooping cough in spite of immunization. *Can J Public Health* 1978;**69**:130-2.
[3] Bennet NM. Whooping cough in Melbourne. *Med J Aust* 1973;ii:481-7.
[4] Eksmyr R. Kikhosta-en öppenvårdsstudie. *Lakartidningen* 1979;**76**:4818-21.
[5] Stewart GT. Vaccination against whooping cough: efficacy versus risk. *Lancet* 1977;i:234-7.
[6] Ditchburn RK. Whooping cough after stopping pertussis immunisation. *Br Med J* 1979;i:1601-3.

****This correspondence is now closed.—ED, *BMJ*.

Effects of pirbuterol and sodium nitroprusside on pulmonary haemodynamics in hypoxic cor pulmonale

SIR,—I would like to take issue with the methodology used by Dr W MacNee and others (22 October, p 1169) for measurement of pulmonary vascular resistance and the effects on this variable of the two drugs pirbuterol and sodium nitroprusside.

The authors state: "Left atrial pressure is not always easy to assess from pulmonary artery wedge pressure in these patients." The formula for measuring pulmonary vascular resistance is therefore invalid, as it includes no estimate of the pressure *difference* across the pulmonary circuit. Whether one believes in the concept of "resistance" in the pulmonary circuit or "impedance," I am sure that most workers would argue that the formula used in this study was wrong.[1 2]

Furthermore, it is not valid to assume that long term administration of pirbuterol had beneficial effects, when no estimate is made of cardiac output. Thus a reduction purely in systolic pressure does not seem clinically important in the pulmonary circuit when there is no estimate of flow through it.

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[1] Foex P. *Pulmonary dynamics*. In: Prys-Roberts C, ed. *The circulation in anaesthesia*. Oxford: Blackwell Scientific Publications, 1980:258-9.
[2] Kaplan JA. Immunodynamic monitoring. In: Kaplan JA, ed. *Cardiac anaesthesia*. New York: Grune and Stratton, 1979-95.

****The authors reply below.—ED, *BMJ*.

SIR,—Dr D W Green is, of course, technically correct. In any segment of the circulation the resistance is defined as the drop in pressure across the segment divided by the rate of volume flow through it. Thus the pulmonary vascular resistance is expressed as the difference between the mean pulmonary arterial pressure and the mean left atrial pressure divided by the cardiac output.

In stating this, however, Dr Green has ignored the controversy that has existed for the past 20 years or more as to whether measurement of pulmonary capillary wedge pressure accurately reflects mean left atrial pressure in patients with severe chronic bronchitis and emphysema, such as those studied in our paper. Fishman states: "Pulmonary capillary wedge pressure and pulmonary diastolic pressure are unreliable indexes of left atrial pressure" in such patients as "either venoconstriction or anatomic change in the intervening vessels may invalidate these measurements."[1] Recent authors support the view that the measurement of pulmonary capillary wedge pressure should be interpreted with caution in patients with disordered pulmonary mechanics,[2] and in such patients "a simple mean of the wedge pressure can be raised secondary to positive intrathoracic pressure during expiration."[3] Although Lockhart has not ascribed the rises in pulmonary capillary wedge pressure in patients with obstructive lung disease to a generalised rise of intrathoracic pressure, close scrutiny of this paper (fig 4) shows a variability of 5 mm Hg between pulmonary capillary wedge pressure and left ventricular end diastolic pressure measured at rest.[4]

It is for these reasons that we chose to measure *total* pulmonary vascular resistance, so avoiding the effect of a possible error in the measurement of resistance. As pulmonary artery pressure in our patients was high and we have assumed that left atrial pressure was low (as all of our patients had well preserved left ventricular function) this is not dissimilar to the approach in calculating systemic vascular resistance, where the right atrial pressure is not usually considered. It was for similar reasons that *total* pulmonary vascular resistance was measured in the MRC long term domiciliary oxygen trial[5] and that the largest single series of measurements of pulmonary haemodynamics in patients with obstructive lung disease does not mention measurements of pulmonary capillary wedge pressure.[6] We cannot therefore agree with Dr Green that "most workers would argue that the formula we used in this study was wrong." We have defined *total* pulmonary vascular resistance (kPa s/cm^5) as the mean pulmonary artery pressure divided by the cardiac output times 8—a definition used by many other workers.[7]

We would also point out that the beneficial effects of long term administration of pirbuterol were based on a reduction of systolic pulmonary artery pressure and an increase in right ventricular ejection fraction. Cardiac output was not measured in order to reduce the number of invasive measurements made during the chronic study. As the increase in right ventricular ejection fraction paralleled the increase in cardiac output during the acute study and as a consistent increase in right ventricular ejection fraction occurred in the chronic study, we have assumed that cardiac output would also increase.

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[1] Fishman AP. *Pulmonary diseases and disorders*. New York: McGraw Hill, 1980:856.
[2] O'Quin R, Marini JJ. Pulmonary arterial occlusion pressure: clinical physiology measurement, and interpretation. *Am Rev Respir Dis* 1983;**128**:319-26.
[3] Rice DL, Awe RJ, Gaasch WH, Alexander JK, Jenkins DE. Wedge pressure measurement in obstructive pulmonary disease. *Chest* 1974;**66**: 628-32.
[4] Lockhart A, Tzareva M, Nader P, Leblanc P, Shcrijen F, Sadoul P. Elevated pulmonary artery wedge pressure at rest and during exercise in chronic bronchitis: fact or fancy. *Clin Sci* 1969;**37**: 503-17.
[5] MRC Working Party. Long term domiciliary oxygen therapy in chronic hypoxic cor pulmonale complicating chronic bronchitis and emphysema. *Lancet* 1981;i:681-6.
[6] Bishop JM, Cross KW. Use of other physiological variables to predict pulmonary artery pressure in patients with chronic respiratory disease. *Eur Heart J* 1981;**2**:509-17.
[7] Morrison D, Goldman S, Wright AL, *et al*. The effect of pulmonary hypertension on systolic function of the right ventricle. *Chest* 1983;**84**:250-7.

Recognising placental steroid sulphatase deficiency

SIR,—The determination of the steroid sulphatase activity in leucocyte homogenates (23 July, p 293)[1] certainly meets the demand for an "easy diagnostic method for X-linked ichthyosis suitable for routine clinical biochemistry laboratories" put forward in the leading article by Dr R A Harkness and others (2 July, p 2). Unfortunately, we observed a considerable variation of the steroid sulphatase activity among obligate carriers of the steroid sulphatase deficiency trait. This limits the ability of our simple method[1] to recognise heterozygotes, which can be needed urgently in cases of low urinary steroid excretion during pregnancy as this may be caused by steroid sulphatase deficiency.

The results of the steroid sulphatase activity determination proved the heterozygosity for this trait in only 14 out of 18 carriers (figure). The much greater variation in the carrier group than in the healthy normal group is not likely to be due to technical differences, as all assays were carried out in the same period by one person.

Scientifically, these results are most interesting as they indicate that no complete escape from X-chromosomal inactivation of the steroid sulphatase locus seems to occur in leucocytes. This, however, differs from the results with cultured fibroblasts initially reported by Shapiro *et al* for four obligate carriers[3] and reported by Müller *et al* for five obligate carriers,[4] which suggested complete escape of inactivation. The reported steroid sulphatase activity in leucocytes[5] and in lymphocytes[6] of normal persons and further work of Shapiro's group on cultured fibroblasts from carriers of the steroid sulphatase deficiency trait[7] indicate, though, a differential expression of the steroid sulphatase locus.